

We Claim:

1. A process for the preparation of hydrated form of amorphous (S)-(+)-Clopidogrel bisulfate comprising
 - 5 i. treating Clopidogrel base with dil. H_2SO_4 in one or more suitable solvent(s);
 - ii. removing the solvent and isolating amorphous form by addition of one or more suitable antisolvent(s).
2. A process for the preparation of hydrated form of amorphous (S)-(+)-Clopidogrel bisulfate comprising
 - 10 i. treating Clopidogrel base in one or more suitable solvent(s) and water with concentrated H_2SO_4 ;
 - ii. removing the solvent and isolating the amorphous form by addition of one or more suitable antisolvent(s).
3. A process for the preparation of hydrated form of amorphous (S)-(+)-Clopidogrel bisulfate comprising
 - 15 i. treating Clopidogrel bisulfate in dichloromethane-water with one or more suitable base(s), to obtain Clopidogrel base;
 - 20 ii. treating the Clopidogrel base(s) with dil. H_2SO_4 in one or more suitable solvent(s);
 - iii. removal of the solvent(s) and isolating the amorphous form by addition of suitable one or more antisolvent(s).
4. A process for the preparation of hydrated form of amorphous (S)-(+)-Clopidogrel bisulfate comprising
 - 25 i. treating Clopidogrel bisulfate in dichloromethane-water with one or more suitable base(s), to obtain Clopidogrel base;
 - ii. treating Clopidogrel base with concentrated H_2SO_4 in a mixture of suitable solvent(s) and water,
 - 30 iii. removing the solvent and isolating the amorphous form by addition of one or more suitable antisolvent(s).

5. A process for the preparation of hydrated form of amorphous (S)-(+)-Clopidogrel bisulfate comprising
- i. treating (S)-(+)-Clopidogrel camphor-sulfonate in one or more suitable solvent(s) with a suitable base(s) to obtain Clopidogrel base wherein the suitable solvent is selected from ethyl acetate, dichloromethane, dichloroethane, chloroform or mixtures thereof
 - ii. treating the Clopidogrel base with concentrated H_2SO_4 in a mixture of one or more suitable solvent(s) and water,
 - iii. removing the solvent(s) and isolating the amorphous form by addition of suitable one or more antisolvent(s).
6. A process for the preparation of hydrated form of amorphous (S)-(+)-Clopidogrel bisulfate comprising
- i. treating (S)-(+)-Clopidogrel camphor-sulfonate in one or more suitable a solvent(s) with one or more suitable base(s), to obtain Clopidogrel base wherein the suitable solvent is selected from ethyl acetate, dichloromethane, dichloroethane, chloroform, or mixture thereof;
 - ii. treating the Clopidogrel base with dilute H_2SO_4 in one or more suitable solvent(s);
 - iii. removing the solvent and isolating the amorphous form by addition of one or more suitable antisolvent(s).
7. A process as claimed in any one of claims 1 to 6, wherein the said suitable solvent is selected from methanol, ethanol, propanol, isopropanol, 1-butanol, 2-butanol, dichloromethane, dimethyl formamide, dimethyl acetamide, 1,4-dioxane, tetrahydrofuran or mixtures thereof.
8. A process as claimed in any one of claims 1 to 6, wherein the suitable antisolvent is selected from pentane, n-hexane, heptane, cyclohexane, pet ether or mixtures thereof.
9. A process as claimed in any one of claims 1 to 6, wherein the suitable base is selected from NaOH, KOH, LiOH, $NaHCO_3$, Na_2CO_3 & K_2CO_3 , organic bases selected from tertiary alkyl amines.

10. A process for the preparation of form I of (S)-(+)-Clopidogrel bisulfate comprising treating Clopidogrel base with dilute H_2SO_4 in one or more suitable solvent(s) and subsequently isolating the crystalline form I from the solvent(s).

5

11. A process for the preparation of form I of (S)-(+)-Clopidogrel bisulfate comprising treating Clopidogrel base with concentrated H_2SO_4 in one or more suitable solvent(s) and water and subsequently isolating the crystalline form I from the solvent(s).

10

12. A process for the preparation of form I of (S)-(+)-Clopidogrel bisulfate comprising dissolving/contacting Clopidogrel bisulfate in any form including crystalline forms II, III, IV, V, VI or any other crystalline forms or amorphous form or in the form of oil with one or more suitable solvent(s) and subsequently isolating the crystalline form I from the solvent(s).

15

13. A process for the preparation of form I of (S)-(+)-Clopidogrel bisulfate comprising treating Clopidogrel bisulfate in any form including crystalline forms II, III, IV, V, VI or any other crystalline forms or amorphous form or in the form of oil is dissolved or contacted with one or more suitable solvent(s) and water and subsequently isolating the crystalline form I from the solvent(s).

20

14. A process for the preparation of form I of (S)-(+)-Clopidogrel bisulfate comprising

- treating (S)-(+)-Clopidogrel camphor-sulfonate in a mixture of a suitable solvent(s) and water with a suitable base(s), to obtain Clopidogrel base wherein the said suitable solvent is selected from ethyl acetate, dichloromethane, dichloroethane, chloroform or mixtures thereof,
- treating the Clopidogrel base with dil. H_2SO_4 in a suitable solvent(s),
- separating the crystals of form I from the solvent(s).

25

30

15. A process for the preparation of form I of (S)-(+)-Clopidogrel bisulfate comprising

- treating (S)-(+)-Clopidogrel camphor-sulfonate in a mixture of a suitable solvent(s) and water with a suitable base, to obtain Clopidogrel base wherein

the suitable solvent is selected from ethyl acetate, dichloromethane, dichloroethane, chloroform or mixtures thereof

- ii. treating the Clopidogrel base with concentrated H_2SO_4 in a mixture of suitable solvent(s) and water
- 5 iii. separating the crystals of form I from the solvent(s).

16. A process for the preparation of form I of (S)-(+)-Clopidogrel bisulfate comprising

- i. treating Clopidogrel base with dil. H_2SO_4 in suitable solvent(s)
- ii. seeding with crystals of form-I
- 10 iii. separating the crystals of form I from the solvent(s).

17. A process for the preparation of form I of (S)-(+)-Clopidogrel bisulfate comprising

- i. treating Clopidogrel base with concentrated H_2SO_4 in suitable solvent(s) and water
- 15 ii. seeding with crystals of form-I
- iii. separating the crystals of form I from the solvent(s).

18. A process for the preparation of form I of (S)-(+)-Clopidogrel bisulfate comprising

- i. treating Clopidogrel camphor-sulfonate in a suitable solvent(s) with a
20 suitable base, to obtain Clopidogrel base wherein the said suitable solvent is
selected from ethyl acetate, dichloromethane, dichloroethane, chloroform or
mixtures thereof;
- ii. treating the Clopidogrel base with dil. H_2SO_4 in a suitable solvent(s)
- iii. seeding with crystals of form-I
- 25 iv. separating the crystals of form I from the solvent(s).

19. A process for the preparation of form I of (S)-(+)-Clopidogrel bisulfate comprising

- i. treating Clopidogrel camphor-sulfonate in one or more suitable solvent(s) with a
30 suitable base, to obtain Clopidogrel base wherein the suitable solvent is selected
from ethyl acetate, dichloromethane, dichloroethane, chloroform or mixtures
thereof
- ii. treating the Clopidogrel base with concentrated H_2SO_4 in a mixture of suitable
solvent(s) and water
- iii. seeding with crystals of form-I

iv. separating the crystals of form I from the solvent(s).

20. A process for the preparation of form I of (S)-(+)-Clopidogrel bisulfate claimed in claim 10 to 20, wherein the said suitable solvent is selected from C₆-C₁₂ alcohols which may be linear or branched, primary, secondary or tertiary alcohols such as hexanol, 2-hexanol, 3-hexanol, isohexanol, heptanol, 2-heptanol, 3-heptanol, 4-heptanol, octanol, iso octanol, decanol or mixtures thereof.
21. A process for the preparation of form I of (S)-(+)-Clopidogrel bisulfate claimed in claim 10 to 20, wherein the suitable base is selected from NaOH, KOH, LiOH, NaHCO₃, Na₂CO₃ and K₂CO₃.
22. A process for the preparation of form II of (S)-(+)-Clopidogrel bisulfate comprising stirring the different amorphous forms in Methyl-tert-butyl ether and subsequent removal of the solvent.
23. A method of treating cardiovascular and related diseases by providing a patient in need thereof, the various forms of (S)-(+)-Clopidogrel bisulfate prepared according to the present invention or pharmaceutical compositions containing the same.
24. Use of the different forms of (S)-(+)-Clopidogrel bisulfate prepared according to the present invention for the preparation of medicine for treatment of cardiovascular and related diseases.